A COMPARISON OF THE IRRITABILITY OF THE VAGUS AND THE SCIATIC NERVES OF DOGS INJECTED WITH METHYL GUANIDIN SULPHATE WITH THYROIDPARATHYROIDECTOMIZED DOGS IN THE TERMS OF RHEOBASE AND CHRONAXIE .

by

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Introduction.

The cause or the causes of the symptoms present due to deficient activity of the Parathyroids glands have been investigated by many workers and from a large number of different angles. Without going into a complete review of the literature, one could briefly summarized the theories as to the causes of the symptoms as follows : -
1. Lack of Calcium ions; 2. Abnormal Phorphorus metabolism; 3. Inorganic ion theory; 4. Alkalosis theory; 5. Interferance of the ammonium metabolism; and 6. the accumulation of the conpoumds of guanidine in the body.

Here, the object was to compare the relationship, if any, of thyroidparathyroidectomized animals to animals which had been injected with Methyl Guanidin Sulphate (M.G.S.) by noting the excitability of the Vagus and the Sciatic nerves.

Histological.

The resemblence of tetania parathyreopriva, idiopathic tetany and guanidin tetany would seem very close by the findings of Paton, Findley, Watson and others (1 to 8) .

Their conclusions relative to tetany following thyroidparathyroidectomy (thyparaect.) are ; - The nervous symptoms are due to the condition of the Central Nervous System,(5); in the production of spasiticity, tremors, and jerkings the cerebral arc is not directly involved . The cerebral arc has a restraining action as shown by decerebration; Integrity of the spinal arc or the cerebellar arcs are not essential for the developement of jerking and tremors. Yet in the advanced stages of the symptoms, there is a disturbance of the sense of equilibrium, which may be due to some involment of the cerebellum .

The same workers have shown that any marked decrease in the amount of parathyroid tissue resulted in amarked increase in the electrical excitability of peripheral motor nerves , indepently of the central nervous system and some increse in the E.E. of the peripheral muscles due chiefly to neural structures.

Evidence presented by these workers cause them to conclude the symptoms of Thyparaect. animals and those produced by the administration of the salts of guanidin are identical, and they are not due primarily to any decrease in the constituents of the body, i.e. calcium. They maintain the parathyroids regulate the metabolism of guanidin in the body, probably by a hormone, and by doing so probably excersise a controling action on the tone of the muscles. Their conclusions of the increase in the E.E. of the nerve are based mainly upon the K.C.C. and the K.O.C. using milliampores as an indicator.

The requirements of an electrical stimulus according to Keith Lucas (10) are intensity and duration. The change in potential must be rapid enought to cause a sufficient change in the irritability of the tissue to start a wave of excitation, Du Bois Reymond Law. This change in the potential be it an increase or a decrease must be of a long enought time interval to overcome any of the interference of the opposite effect of the make or of the break .

Working on this hypothesis that the requirements were a sufficient voltage and a sufficient time interval duration, Lucas (10) developed a means of measuring these by means of a voltmeter and a pendulum for making and breaking the circuit during its arc .

Waller (11) used condenser discharge for measureing the time interval. Yet Lapicque, quoting Fulton (11 -12) , was instrumental in the developement of the condensers discharge method o f measuring time intervals . His apparatus is decribed in full by Fulton (11 - 12) and enables one to measure accurately the intensity and the time interval of the discharge.

Lapicque has formulated the words Rheobase and Chronaxie to designate the strength and the time interval of current used. His definition (13) of these terms are ; rheobase is the intensity in voltage of a constant current closed instanteously which will just excite if it is continued indefinitely, chronaxie is the time of current flow required to result in an excitation by a current of intensity just double the rheobase.

Noyons (9) with the condenser discharge method resembling Lapicque,measures the E.E. in volts. His method consists in using constant time durations and measuring the voltage necessary to bring about a response for these various constant time intervals. His observations give results which agrees with those of Lapicque.

Using apparatus similiar to Lapicque,as is described in Fulton (11 - 12), Buchanan and Garven (15) have studied the rheobase and chronaxie of the sciatic nerves in tetany due to thyparaect. and in tetany due to the administration of methyl guanidin . They observe that there is a daily variation in both the rheobase and the chronaxie . The variation in the rheobase was the most marked of the two. Following the administration of Methyl guanidin sulphate , there was no change in the rheobase, and a slight fall in the chronaxie ; while following thyparaect. the rheobase diminished and the chronaxie increased . In the latter group of dogs, they found the change more marked in the nerves than in muscles . The severity of the symptoms and the amount of change in the rheobase and the chronaxie did not necessarily correspond ; usually the chronaxie increasing following thyparaect., followed by a fall and then an augmentation just before death.

These results leads them to conclude that tetany following thyparaect. and tetany following the injection of methyl guanidin sulphate are not closely related, which differs with the conclusions of Paton, Findley, and other (1 to 8) .

Relative to whether thyparaect. results in any change in the amount of methyl guanidin salts in the blood , the observations seem to be still at variance. Paton and Sharpe (14) find an increase in guanidin while Greenwald does not find any increase (15) . Their failure to check seems to be a question of finding a positive method of determing guanidin accurately.

Additional evidence in support of the resemblence tetany caused by the removal of the parathyroids and that following the administration of guanidin compounds is that of Susman $16) who by repeated small injections into animals of guanidin showed a depletion of the fat droplets of the parathyroid glands which would correspond to their increased activity. Susman(16) found that hypertrophy and hyperplasia of these glands could be induced by small daily injections of guanidin.

Working independently Hammett (17) and Appleton(28) have demonstrated a hypertophy of the submaxillary glands caused by deficient parathyroid activity , which results in increased activity of the salivary glands . Injection of guanidin has been shown to cause increase salivation by many investigators.

The decrease of Vagus activity following guanidin injections (intravenously) and after the removal of the parathyroids has been noted by Burns and Watson (19) . They state the methyl guanidin seem to have the more marked effect of the two. Their work seem to show the seat of this effect seems to be first at the synapses and then the terminal endings. Calcium Lactate removes this effect. They report there seems to be no effect on the sympathetic nerves as a results of intravenous injections.

The decrease of Calcium ions in the blood after the removal of the parathyroids have been pointed out by many as a factor causing the symptons. It has been demonstrated that a decrease of calium ions does occur as an result of the removal of the parathyroids. The increase of irritability of tissues placed in diminished concentration on Calcium was observed by Bouchaert and Colle (20). The rheobase decreased while the chronaxie increased. It was also shown (20) that when tissues were placed in increased concentrations of Calcium the rheobase is increased and the chronaxie is lowered.

Lapicque found similiar result with calaium ions on the heart. A decrease of calcium ions causing a decrease of the rheobase, (21).

Whether the nerve is cut or not, the increase in its irritability has been demonstrated to occur when the calcium is decreased, after guanidin injection, and following the removal of the parathyroid glands. H. Fuhner (22) found guanidin had no effect on muscles after their nerve was cut and allowed to degenerate.

Paton, Findley (2) have obtained similiar results following curarization.

Jung(23) maintains there must be evidently a parathyroid hormone, which would exhibit the properties or functions of the parathyroids.

Lucas (24) finds the ventricular muscle of the frog to have a chronaxie of 0.08 seconds using fluid electrodes, which of course would completely cover the heart, making his electrodes large . Adrian (25) with pore electrodes where the different electrode is pointed or not pointed observed that the chronaxie of the ventricular muscle of frogs had a chronaxie of 0.005 second . Lapicque and Veil (26) with electrodes similiar to Adrian's found a double chronaxie; 0.0055 and 0.1 second . Adrian (25) and Davis (27) have suggested that the difference is due to the size of the electrodes. A larger electrode will cause one to obtain a larger chronaxie .

Lucas, Adrian, and Lapicque as stated by Fulton(12) and Adrian(25) found the further apart the electrodes the smaller the chronaxie. The biggest change is obtained in increasing the separating distance up to 20 mm. An increase beyond this does not shorten the chronaxie materially. Rushton (14) showed the rheobase varies inversely with the cosine of the angle found betweem the nerve and the direction of current flow ; namely the more perpendicular the larger the rheobase.

Von Bezold according to Lapicque (29) finds an increase in the strength of current over the rheobase or in other words if too high of a rheobase reading is taken , the chronaxie reading will be less than the correct chronaxie.

The rapidity of the establishment of the flow of the current according to Lapicque (29) have been shown by Du Bois Reymond to affect the intensity necessary for excitation to occur, and by Brück and Fick working separate to affect the chronaxie.

(30) observed that starting from a minimal frequency which causes no change in threshold an increase in frequency causes a decrease in the effective voltage,owing to latent addition , up to a certain point beyond which there is no change due to the refractory period.

A review of the literature shows additional characteristics of the chronaxie relation to the electrical irritability. Lapicque and Legendre (31) and Oinuma (32) show the chronaxie of the nerve multiplied with the square of the diameter of that nerve is usually near a given number for that species of animals.

Laugier (33) has demonstrated that extraction of water from a tissue causes a lowering of the rheobase and an increase in the chronaxie, by means of the application of hypertonic salt solution .Lapicque and Legendre (34) have shown that a swollen nerve has an increase rheobase and a decrease chronaxie and that anesthesias using locals such as cocain, scopolamine, or ether, or in general using ether, chloroform, or morphine the nerves will become swollen which results in an increase rheobase and a decrease chronaxie. Lapicque in a demonstration found a lower chronaxie than normal and has since shown that this was due to a cold temperature which he found to cause a swelling of the nerves. Buchman and Garven (15) state that ether has an

Marked affect upon the rheobase and chronaxie determinations. They found ether to have an augumentative affect upon both the rheobase and the chronaxie, which returns to normal in 3 to 6 hours after the withdrawal of the anesthetic, falling below normal for a few hours, but is always back to normal before 12 hours. Paton, Findley, and others (3) find ether to cause a transient increase in the E.E. followed by a slow progressive decrease.

Guanidin increases the permeability of red corpuscles as shown by Secker (35) due to afall in the glucose and clorides in plasma . Nothing has been read as to whether it causes any increase or decrease of water .

The muscle fibers tend to have the same chronaxies which the nerves have that innervates them. This was demonstrated by the Lapicques (12), who call it a condition of isochronism . Any condition which will bring about a difference of 100 % in the chronaxies of a nerve and the muscle it innervates will cause a block.

Theoretically this could be produced in any of the following four ways : - Chronaxies of

1. muscle augmented, nerve unaffected as in the action of c curare ;

2. muscle unaffected, nerve diminished - action of strychnine;

3. muscle diminished, nerve unaffected - action of nicotine, veratrin, physostigma;

4. muscle unaffected, nerve augmented .
At present no substance with an action of the fourth type is known. Hypertonic salt solution augments the chronaxies of both the nerve and the muscle.

It follows from Lapicque theory that any drug which causes a blocking by a decrease in the chronaxie of the muscle should be counteracted by a drug which will augment the chronaxie of the muscle or also by any drug which will diminish the chronaxie of the nerve so as to eliminate any difference between the chronaxies of a muscle and the nerve which innervates it. From this, the block caused by curare should be removed by the action of veratrin, nicotine, or physostigma as well as by one of the fourth type. The capacity of removing a block by bringing the chronaxies of a muscle and nerve into isochronism has been demonstrated by the Lapicques (12).

Procedure and
Description of Apparatus

The apparatus used for these experiments was essentially similiar to that described by Fulton (11-12) as used by Bapicque and others. The range of voltage was to 270 in the condenser circuit. Non polarizable AgCl coated silver electrodes of mm. in diameter were used; placed on the nerve at the same angle always , the flow of the current being parallel to the nerve. These electrodes were held in a"Bakelite" shield.

The electrodes were a constant distance apart , 22 mm., being fixed in the shield, and arranged so there was little possibility of tissue fluid or blood short-circuiting them.

For the deliverance of single stimuli , a sliding contact was used ; and the making of the circuit was practically always at the same rate of speed being nearly instanteous. For the delivering of a tetanizing current an electric tuning fork,which vibrated at the rate of 82 times per second,was used to deliver stimuli at the rthym of 82 per second. The end of the fork ~~xxx~~ , insulated from the fork proper , was connected to the condensers . It vibrated thru an arc of 5mm. , making contact with the batteries at one end of its stroke for a length of time sufficient to charge the condensers; and making contact with the leads to the electrodes at the other end of its stroke, of course after it had broken the contact with the batteries and swung thru its arc. In this way the condensers are charged and then discharged 82 times per second.

To eliminate any chance of an error in the intensity of the rheobase which would result in an incorrect chronaxie , the rheobase was determine before and after the chronaxie determinations.

The apparatus was checked with Lapicque's and other by checking his results in the chronaxie determination of frogs' nerves and muscles, as well as the action of curare.

A condition noticed yet never found in literature was the Rheobase read was not the actual intensity of the current delivered to the electrodes. The resistances of 7,000 and 10,000 ohms and the shunt of 3,000 ohms is really an additional potentiometer which allows only 0.1 of the intensity read to be the stimulus.

In light of some of the earlier experiments the condition was noted that any error in the rheobase resulted in an error in the chronaxie in the opposite direction. This would tend to show the presence of a constant as the requirement of a stimulus as well as the requirements put forth by Lucas (10) . Deriaud in his articlex(37) and others have made efforts to find the constant. An Additional reading was taken in several of the animals which consisted in measuring the minimun excitation time that would cause a maximun response for that intensity. For convenience this will be called the maximal stimulus of excitation time .

Observations have been made upon 35 frogs and upon 30 dogs in addition to those used to check the apparatus and the technic .

Tabulations and Charts of Results.

The animals used in these experiments could be divided into groups according to the observations made upon them.

GROUP I. Observations made upon animals without any influence of ether; # 25 , 29 , 27 , 16 , 19 , & 20.

GROUP II. Those injected subcutaneously with methyl guanidin sulphate ; # 25 , 13 , 29 , 30 , 28 , 14 , 19 on composite chart, and 17.

GROUPS III. Animals given M.G.S. intravenously; 1 , 2 , 3 , 4 , 5 , 6, 7 , 12 , 13 , 14 , 16 , 19 , 20.

GROUP IV. Thyroidparathyroidectomized Dogs ; # 21 , 22 , 23 , 24 , 26 , 27 . X

GROUP V. Calcium Lactate administered after the injection of guanidin ; # 17 , & 29 ; after removal of the parathyroids ; 22 , & 26.

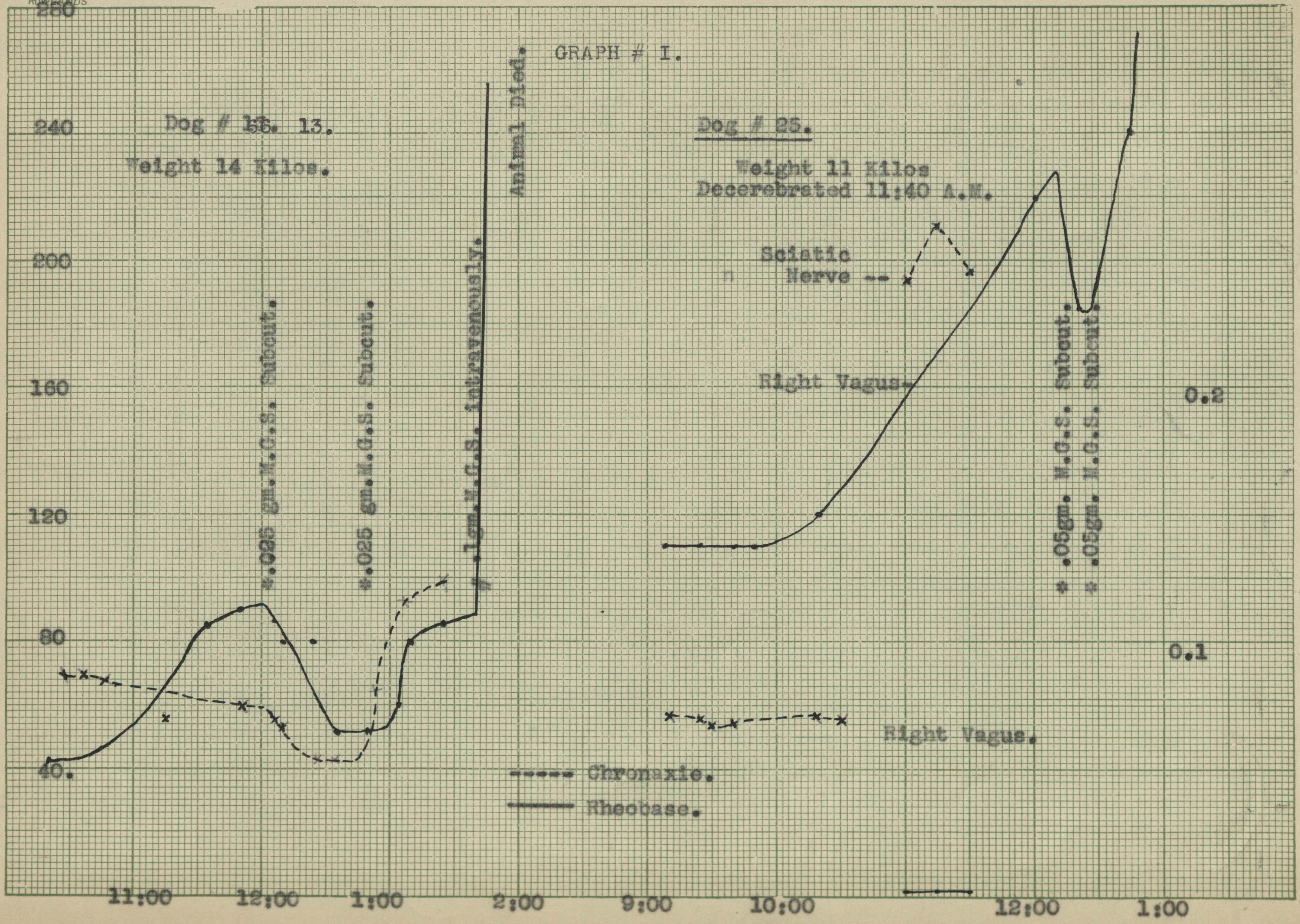
GROUP VI. Animal given M.G.S. following the parathyroids removal ; #21 .

Group VII. Animals of the above groups that showed an augmentation of the rheobase of the Vagus following its separation from the C. N. S. ; # 25 , 28 , 13 , 21 , 24 , & 29 .

Group VIII. Dogs in the above groups that belonged to the same litter ; 26 , 29 , 28 , & 30 .

Group IX. Dogs not given ether, and given M.G.S. either subcutaneously or intravenously .

Group X. Frogs used for the action on muscles & nerve.



GRAPH # I.
Dog # 16. 13.
Weight 14 Kilos.
*.025 gm.M.C.S. Subcut.
*.025 gm.M.C.S. Subcut.
.1gm. M.C.S. Intravenously.
Animal Died.
Dog # 25.
Weight 11 Kilos
Decerebrated 11:40 A.M.
Sciatic
Nerve
Right Vagus.
* .05gm. M.C.S. Subcut.
* .05gm. M.C.S. Subcut.
Right Vagus.
Chronaxie.
Rheobase.
280
240
200
160
120
80
40.
0.2
0.1
11:00
12:00
1:00
2:00
9:00
10:00
12:00
1:00

Dog # 25.

Female , weight 11 Kilos.

Decerebrated April 26, 1928. 10:30 to 11:45 A.M.

Ether was withdrawn at 11:40.

Graphs started at 8:30 and taken till 12:00 midnight.
Right Vagus ligated at 8:50.

	Right Vagus.			Sciatic Nerve.	
Time	Rheobase	Chronaxie	Response	Rheobase	Chron axie.
9:10	150	0.259 ∝	M.B.		
9:10	110	0.07- "	6 mm. fall.		
9:25	110	0.07 "			
9:30	110	0.068 "			
9:40	110	0.07- "			
9:50	110	0.07- "			
10:20	120	0.07 "			
10:30	120	0.07 "			
11:00				1.5	.2407 <
11:15				1.5	.2601 "
11:30				1.5	.2407 + "
12:00	220				
12:10		0.05 grams of M.G.S. per Kilo. subcut.			
12:20	185				
12:23		0.05 grams of M.G.S. per Kilo. subcut.			
12:30	220				
12:45	240				
12:55	270 above this.				

1:00 Animal died of respiratory failure.

M.B. is missed beat of the heart.

Dog # 13.

Weight - 14 Kilos. Female.

Performed 4/24/1928.

Ether started at 9:20 A.M. Electrodes placed upon the L.Vagus nerve 9:45 A.M.

Vagus tied at 10:15 caused a rise of 16 mm. in the Blood Pressure showing that the Left, Vagus was active.

In making the following determinations the stimula was applied for 10 seconds.

Time	Rheobase	Chronaxie	Maximal Stim.	Injection
10:20	43 Volts	0.0822	0.207 to o.24	
11:15	80	0.07		
11:35	85		0.24-	
11:50	90	0.074		
12:00				0.025 grams of M.G.S. per Kilos. Subcut.
12:06	86	0.07		
12:10	80	0.068-		
12:25	80	0.061	caused the heart to miss beat	
12:35	52	0.061	" " " " " "	
12:45				0.025 grams of M.G.S. per Kilo. Subcut.
12:50	52	0.08		
1:05	60	0.148-		
1:10	80	0.1156 +		
1:25	85	0.123 +		
1:40				0.1 gram M.G.S. per Kilo. intravenously
1:42	Over 100			
1:44	Over 185			
1 :55		Animal Died.		

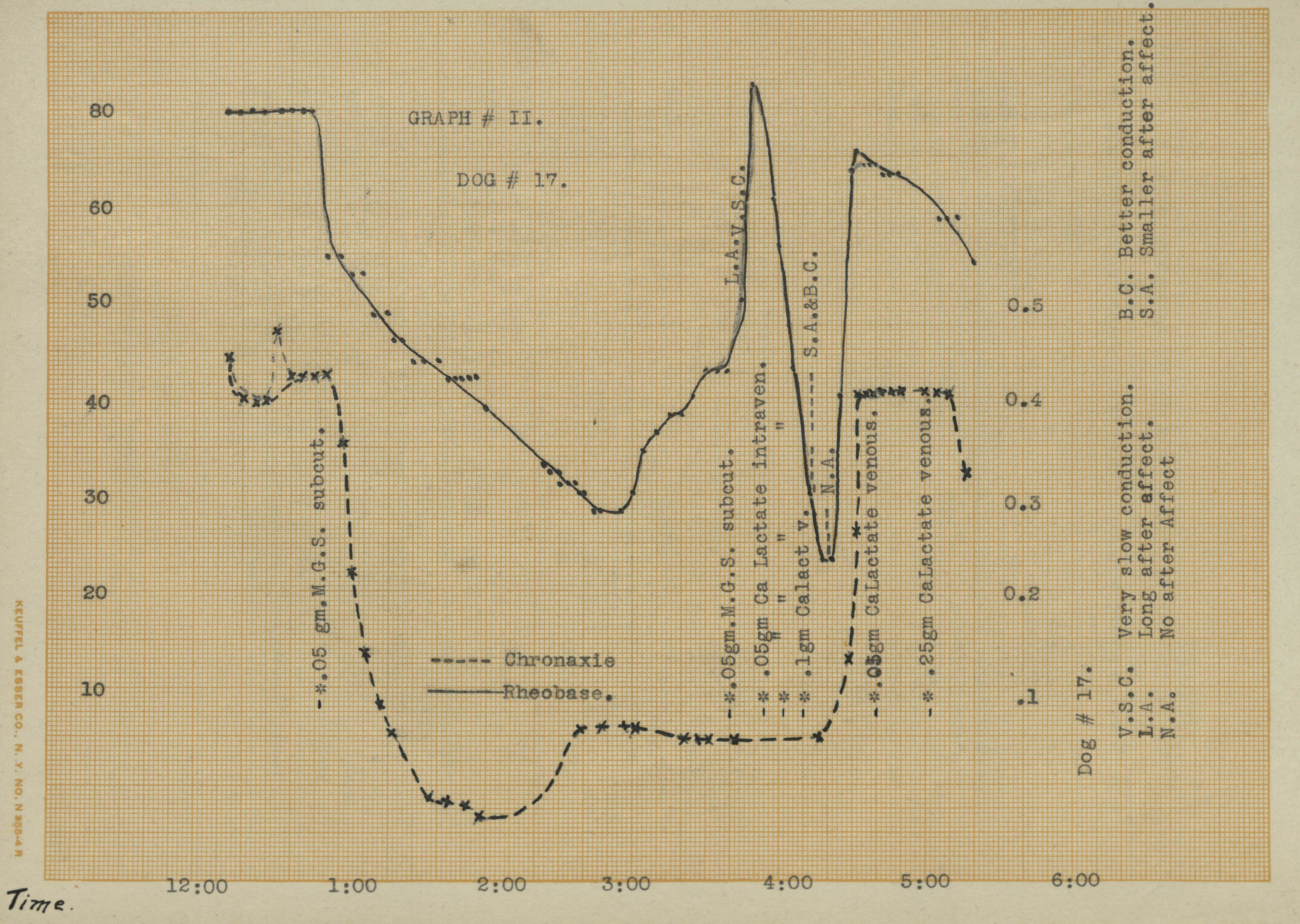
SUBCUTANEOUS INJECTIONS.

COMPOSITE CHART.

DOG.	Just before Injection	Gms. inj. per Kilo	Determinations.
25	R. - 220.	0.05	9" R - 185.
13	R. - 90. C. - .074	0.025	6" 86. .07 10" 80. .068 25" 80.* .061* 35" 35* .061*
	45"	0.025	5" 50. .08 15" 60. .148- 20" 80 .1156
29.	R. - 81. C. - .03 160. - No M.B.	73. 0.05 0.1	5" 73 15" 82. .240 5" 82.* .240* 20" 149. slight.
	Other Vagus.		15" 42* .185* 20" 49 .185 30" 60. .123
30.	R. - 140* C. - .240* R. - 92. C. - .185 R. 83. & C. .148 &	0.05	3" 111.* 28" 76.* .064 * 4" 80. .185 8" 68. .185- 18" 62. .148
28.	R. - 102.& C. - .148 &	0.05	20" 92. * 60" 75. * .064 *
14.	R. - 225.	0.05	1" 212. 12" 225.* 20" 160.*
19.	R. - 50. C. - .03	0.05	32" R.- 44. C.-.07-

- * = M.B. &.= Slight action. " = minutes after Inj.

R = Rheobase in Volts. C. Chronaxie in Sigma Seconds.



GRAPH # II.
DOG # 17.
80
60
50
40
30
20
10
0.5
0.4
0.3
0.2
.1
12:00
1:00
2:00
3:00
4:00
5:00
6:00
Time.
*.05 gm.M.G.S. subcut.
*.05gm.M.G.S. subcut.
*.05gm Ca Lactate intraven.
* " "
* " "
*.1gm Calact v.
*.05gm CaLactate venous.
*.25gm CaLactate venous.
L.A.V.S.C.
S.A.&B.C.
N.A.
----- Chronaxie
——— Rheobase.
Dog # 17.
V.S.C. Very slow conduction.
L.A. Long after affect.
N.A. No after Affect
B.C. Better conduction.
S.A. Smaller after affect.
KEUFFEL & ESSER CO., N. Y. NO. N 355-4 R

Dog # 17.

Female Spitz, Weight 6.6 Kilos.

Experiment performed May 5th, 1928, on Left Vagus.

Ether started at 10:30 A.M.

Time	Rheobase	Excit. Time in	Seconds that Stimula applied	Chronaxie.	
10:45	117.	0.3.	7.		
10:50	125.	0.3.	5.		
10:55	125.	0.266	12.		
11:10	93.	0.74	12.		
11:15	93.	0.888	7.		
11:17	81.	1.48	8.		
11:18	81.	1.85	5.		
11:20	72.	1.85 -	10.		
11:25	68.	3.33	8.		
11:29	63.	3.33 -	18.		
LL:35	68.	2.69	12.		
11:40	64.	3.33	10.	0.148	4.
				0.123	15
				0.1257	8
11:55	75.	~~0.0822~~	~~4~~	0.0822	4
	78.	~~0.0822~~	~~3.~~	0.0822	3.
	75	~~0.0822~~	~~8.~~		
12:00	77			to cause a M.B.	
12:15	80		11.	0.429	13.
12:20	80		12	0.4	14
12:25	80		12	0.4	14.
12:30	80		2		
12:35	80		½	0.46	½/
12:40	80			0.42	
12:45	80			0.42	
12:50	80			0.42	
12:52		0.05 gram of M.G.S. per Kilo subcut.			
12:55	65			0.42	
1:00	65			0.37	
1:05	63			0.258	
1:10	63			0.185	
1:15	59			0.148	
1:20	59			0.123	

Dog # 17 continued.

Time	Rheobase	Chronaxie
1:22	56	0.107-
1:25	56	
1:30	54	
1?35	54	0.074
1: 40	54	
1:43	52	0.07
1:45	52	
1:50	52	0.061
1:55	52	0.053
2:00	49	
2:05	65 &0.148 =	
	72 & .123 =	
	104 & .053.	
2:10	47	0.074
2:15	82 & .1156 =	
	77 & .123 =	
	88 & .0925 =	
	94 & .074 =	
	75½& .148 .	
2:28	43	
2:25	42	0.1156
2:30	42	0.1156
2:33	41	0.1156
2:35	41	
2:38	40	0.1257
2:40	40	
2:45	38	0.1257
2:48	38	
2:55	38	0.1257
3:00	40	
3:05	44	over 0.123
3:10	46	" 0.123
3:15	48	
3:20	48	0.1156
3:25	50	0.1156
3.30	52	0.1156
3::35	52	0.1156
3:40	0.05 gram of M.G.S. per Kilo. subcutaneously.	

Time	Rheobase	Chronaxie.
3:45	60	
	Vagus has slow conduction and long after affect.	
3:50	82	0.1156
	Very slow conduction and longer after affect than 5 min. ago.	
3:55	Injection of Calcium Lactate	
3:58	70	
4:00	65	
	Better conduction and less after affect.	
4:02	Calcium Lactate inj.	
4:04	60	
	After affect gone, conduction O.K.	
4:05	52	
4:10	Calcium Lactate 0.1 gr. per Kilo intraven.	
4:11	40	
4:15	32½	0.1156
4:20	33	
4:25	49	
4:28	73	0.185
4:30	74	0.3-
4:33	75	0.4
4:35	74	0.4
4:38	74	0.4
4:40	74	0.4
	0.05 gr Ca Lactate per Kilo imtravenously.	
4:42	73	0.4
4:45	73	0.4
5:00	90	0.4
5.02	Ca. Lactate 0.025 gr.	
5:05	68	0.4
5:15	68	0;4

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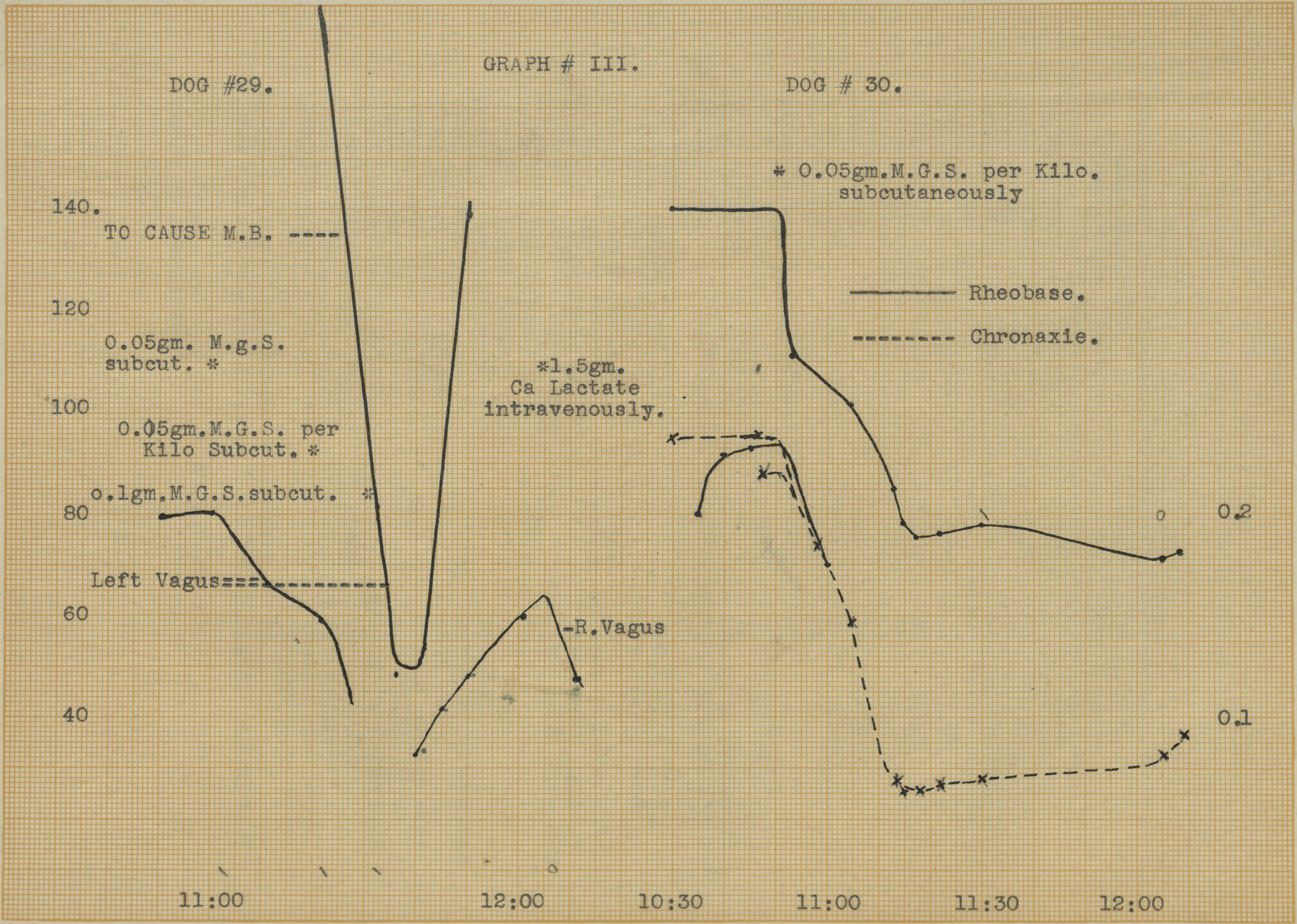


GRAPH # III.
DOG #29.
DOG # 30.
* 0.05gm.M.G.S. per Kilo.
subcutaneously
140.
TO CAUSE M.B. ----
120
0.05gm. M.g.S.
subcut. *
*1.5gm.
Ca Lactate
intravenously.
100
0.05gm.M.G.S. per
Kilo Subcut. *
o.1gm.M.G.S.subcut. *
80
Left Vagus===---------
60
-R.Vagus
40
Rheobase.
Chronaxie.
0.2
0.1
11:00
12:00
10:30
11:00
11:30
12:00
KEUFFEL & ESSER CO., N. Y. NO. N 355-4 R

Dog # 29.

Terrior Pup, Female, Weight - 4. Kilos.

Experiment performed May 10, 1928.

Ether started at 10:40 A.M.

	Left Vagus			Right Vagus.	
Time	Rheobase	Chronaxie	Response	Rheobase	Chronaxie
10:50	81	0.3 =	slight		
10:52	160		no missed beat		
11:10		0.05 gram per Kilos. subcutan. (M.G.S.)			
11:14	160		no missed beat		
11:18	81	0.3	better		
11:20		0.05 gram of M.G.S. per Kilo. subcutaneously			
11:25	81		still better fall		
11:28	160		no missed beat		
11:30		0.1 gram of M.G.S. per Kilo. Subcutaneously.			
11:35	82	0.240	missed beat		
11: 40			" "	34.	
11:45			" "	42.	0.185
11:50	149	= (slight)	" "	49	0.185
12:00			" "	60	0.123
12:05		1.5 gram of Ca. Lactate per Kilo intraven.			
12:10			missed beat	48	0.148.

One of the Dogs in Group L .

Dog # 30.

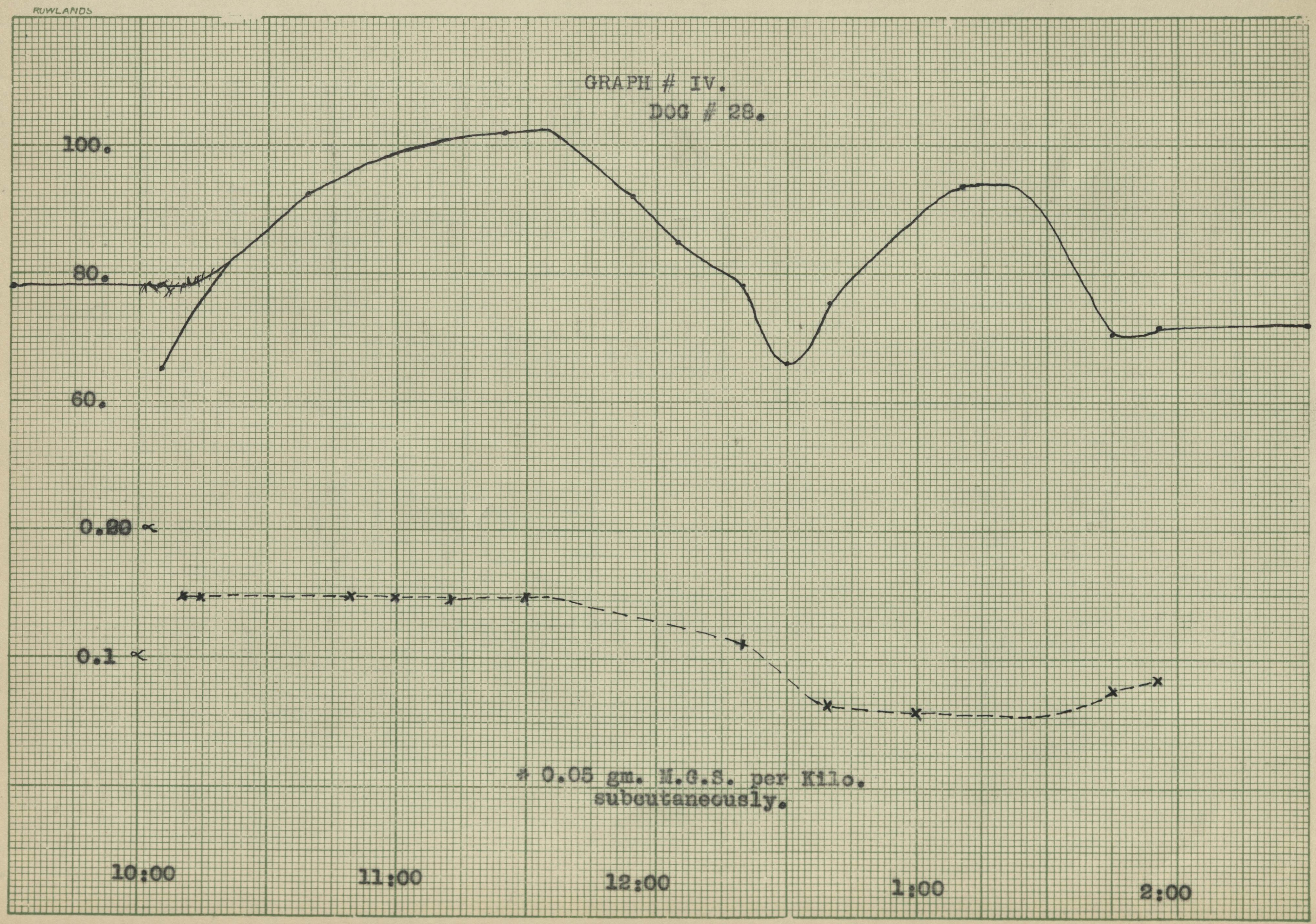
Weight 5. Kilos. Terrior.

May 15, 1928.

Time	Left Vagus. Rheobase	Chronaxie	Response.
10:10	140	.240	Missëd Beat.
10:20	83	.148	Very slight.
10:40	90	.185 -	8 to 10 mm. fall.
10:50		0.05 gm. M.G.S.	per Kilo. subcutan.
10:53	111		Missed Beat.
10:54	80	.185	8 to 10 mm. fall
10:58	68	.185	" " " .
11:05	83	.148	16 mm. fall.
11:08	62	.148	8 to 10 mm. fall.
11:13	85		Missed Beat.
11:15	78	.07	" " .
11:18	75½	.064	" " .
11:22	76	.064	" " .
11:30	78	.068	" " .
11:32	96	.074 -	" " .
12:05	72	.0925	" " .

****

One of Dogs of the group L.



RUWLANDS
GRAPH # IV.
DOG # 28.
100.
80.
60.
0.20 ∝
0.1 ∝
0.05 gm. M.G.S. per Kilo.
subcutaneously.
10:00
11:00
12:00
1:00
2:00

Dog. # 28.

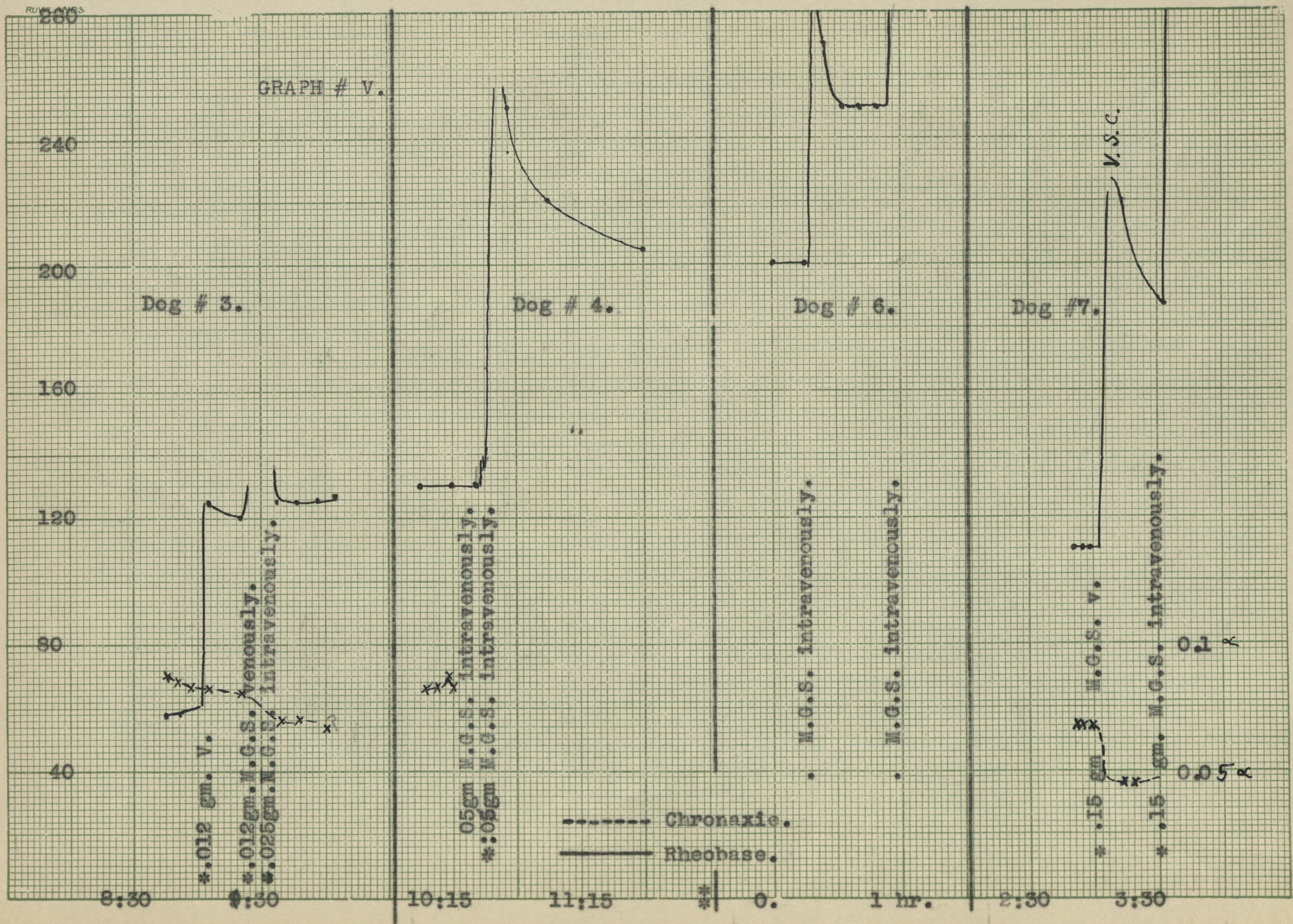
Female , Weight 3.8 Kilos. Terrior.

Experiment performed May 7, 1928.

	Left Vagus.		
Time	Rheobase	Chronaxie	Response.
(9:50)	Ether started.		
10:10	65	0.1485	3.mm fall.
10:35	93	0.148	3. mm fall.
10:40	95	0.148	3. mm fall.
11:25	102	0.148	3. mm fall.
11:35			
	0.05 gm of M.G.S. subcut. (per Kilo.)		
11:55	92		Missed Beat.
12:05	85	0.148-	" " .
12:20	78	0.1156	" " .
12:30	66	0.1156-	" " .
12:40	75¾	0.064	" " .
1:00	84	0.061	" " .
1:10	94		" " .
1:55	72	0.0825 -	" " .

****

One of the Dogs of Group L.


GRAPH # V.
280
240
200
160
120
80
40
Dog # 3.
Dog # 4.
Dog # 6.
Dog #7.
*.012 gm. V.
*.012gm.M.G.S. venously.
*.025gm.M.G.S. intravenously.
.05gm M.G.S. intravenously.
*.05gm M.G.S. intravenously.
M.G.S. intravenously.
M.G.S. intravenously.
V.S.C.
* .15 gm. M.G.S. V.
* .15 gm. M.G.S. intravenously.
0.1 α
0.05 α
Chronaxie.
Rheobase.
8:30
9:30
10:15
11:15
0.
1 hr.
2:30
3:30

Dog # 3.

Male Weight 19 Kilos.

Performed December 22, 1927.

Time	Vagus. Rheobase	Chronaxie	Response.
8:45	55 Volts.	0.09—	slight fall.
9:00	0.012 grams of M.G.S. per Kilo. intravenously.		
9:05	125.	0.07 -	Missed Beat.
9:10	125.	0.080	2 " " .
9:20	125.	0.08-	" " .
9:22			
9:22	0.012 grams of M.G.S. per Kilo. intravenously.		
9:25	125.	0.08	Slight fall.
9:30	0.025 grams of M.G.S. per Kilo. intravenously.		
9:33	125.	0.07	very slight fall.

****

Dog # 4.

Male Weight 20 Kilos.

Performed January 6, 1928.

Time	Left Vagus . Rheobase	Chronaxie	
10:00 Ether Started.			
10:15	130	0.082	Missed Beat.
10:25			
10:25	0.05 gm. of M.G.S. per Kilo. intravenously.		
10:27	Over 130		
10:33	0.05 gm. of M.G.S. per Kilo. intravenously.		
10:40	270.	-	
11:00	220.		
11:30	205.		

****

Dog. # 6.

Time	Vagus. Rheobase	Chronaxie.	
0.hr.0 min.	220		good response.
15 min.	220		gOOd response.
16 min	M.G.S. injected intravenously.		
19 min	above 270.		
26 min.	250		fair response.
33.min.	250		better response.
38 min.	250		good response.
50 min.	M.G.S. injected intravenously.		
55 min.	above 270	sluggish in action.	
56 min.	M.G.S. injected intravenously.		
60 min.	above 270	more sluggish.	

****

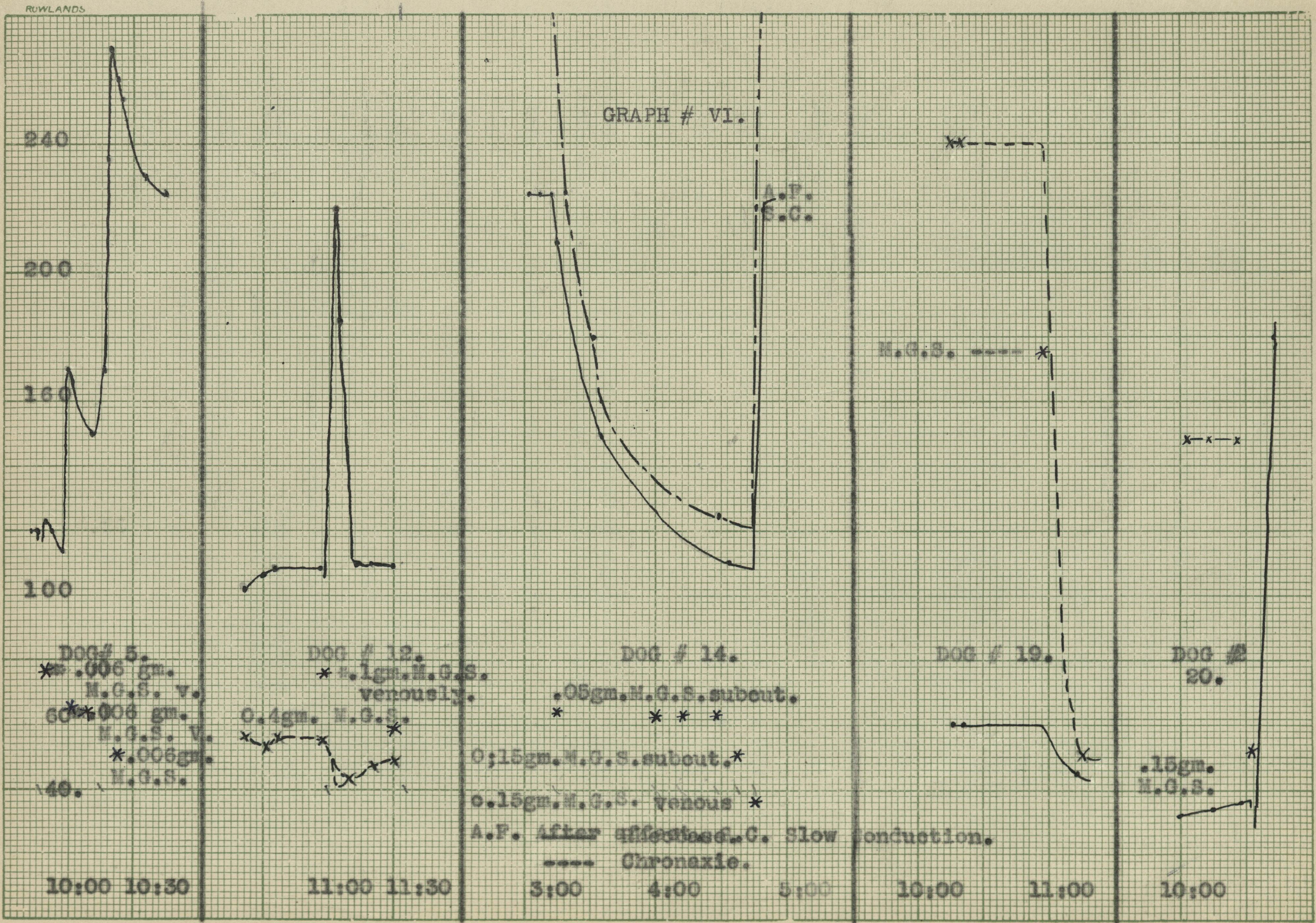
Data sheet on this animal was misplaced.

Dog # 7.

Female Weight 13 Kilos.
Experiment performed January 31, 1928, Right Vagus.

Time	Rheobase	Chronaxie	Response.
2:40	Ether started/		
2:55	110.	0.07---	M.B. 25 mm. fall.
3:00	0.15 gm. M.G.S. per Kilo. intravenously.		
3:01	110		No response.(slight)
3:02	220		No M.B. 12. mm. fall.
3:04	170		No M.B. 10. mm. fall.
3;08	220		M.B. 35 mm. fall.
3:10	220		M.B. 35 mm. fall.
3:18	115		M.B. 15 mm. fall.
3:19	110		No M.B. 10 mm. fall.
$;19		0.07------	M.B. 88 mm. fall
3:20		0.07------	M.B. 50 mm. gall.
3:23	110.		No M.B. 12 mm. fall.
3:85			
3:30	0.15 gm.M.G.S. per Kilo. intravenously.		
3:32	220		14 mm. fall .
#;40	220		10 mm. fall .

****



ROWLANDS
GRAPH # VI.
240
200
160
100
60
40.
DOG# 5.
.006 gm.
M.G.S. V.
.006 gm.
M.G.S. V.
.006gm.
M.G.S.
DOG # 12.
.1gm.M.G.S.
venously.
0.4gm. M.G.S.
DOG # 14.
.05gm.M.G.S.subcut.
0;15gm.M.G.S.subcut.
o.15gm.M.G.S. venous
A.F. After effectsS.C. Slow conduction.
---- Chronaxie.
A.F.
S.C.
DOG # 19.
M.G.S. ----
DOG #2
20.
.15gm.
M.G.S.
10:00 10:30
11:00 11:30
3:00
4:00
5:00
10:00
11:00
10:00

DOG # 5.

Male. Weight - 11 Kilos.

Experiment performed Jan. 7 , 1928.

Ether started at 9:25.

	Left Vagus.	
Time.	Rheobase	Chronaxie.
9:40	120. Volts	0.074
9:45	120.	0.074
9:47	0.006 gm. M.G.S. per Kilo. intravenously.	
9:50	120.	0.082
9:55	120.	
9:57	0.006 gm. M.G.S. per Kilo. intravenously.	
9:59	170.	0.0822
10:10	150.	
10:15	0.006 gm. M.G.S. per Kilo. intravenously.	
10:16	170.	
10:16½	170.	
10:18	235.	
10:29	270.	
10:30	248.	
10:35	230.	
10:45	225.	

****

DOG # 12 .

Female Weight 15 Kilos.

Experiment performed Feb. 15 , 1928.

Time	Right Rheobase	Vagus. Chronaxie.	
10:00	Ether started.		
10:35	108. Volts.	0.07-	
10:57	108;	0.07-	
10:59	0.1 gm. M.G.S. per Kilo. intravenously.		
11:01	180. gives very little response.		
11:01½	220.		
11:02.	220. same response as 108 at start.		
11:03	185.	0.07 ---	
11:10	110.	0.0536	estimated
11:20	109.	0.05 -	
11:35	0.4 gm. M.g.S. per Kilo. intravenously.		
11:35½	No response at 270 Volts.		

****

Dog #. 14.

Female, Weight 12.5 Kilos.

Experiment performed February 29. 1928.

Time	Left Vagus Rheobase	Chronaxie	Response	Left Sciatic Rheobase	Chronaxie.
2:45		Ether started.			
3:11			2 -	15	
			3 -	18	
3:12			4 -	25	
			2 -	15	
			0	12	
3:13			0	13	
			2 -	15	
3:14	228		8. mm fall		
	225		8. mm "		
	225		8.mm "		
3:15	0.05 gram of M.G.S. per Kilo. subcutaneously.				
3:15½	225		25 mm fall (missed beat)		
3:16	210		6 mm "		
	220		12 mm. "		
3:16 ½			3 -	15	
			3 -	15	
3:27	225		25 mm. fall (missed beat)		
3:30	225		25 mm. " " "		
3:33	180		25 mm. " " "		
3:35	160		27 mm. " " "		
3:36	140		6 mm. "" None.		
3:37	160		20 mm. " (Missed beat)		
3:38			3 -	15	
3:39			2 -	12	
3:50	180		nothing		
3:53	225		very slight.		
4:00	0.05 grams ogfM.G.S. per Kilo. subcutaneously.				
4:01	180		nothing		
	220		8. mm fall.		
	180		1.3 mm. " .		
4:02			3 -	25	
			2 -	20	
4:06	220		7. mm. fall.		
			3 -	20	
4:08			2-	15	
4:10	220		10 mm. fall.		

Dog #. 14 Continued,

Time	Left Vagus Rheobase	Chronaxie	Response	Sciatic. Rheobase	Chronaxie
4:12	0.05 gram of M.G.S. per Kilo. subcutaneously.				
4: 25	160		32 mm. fall. (missed beat)		
4: 25½	140		28 mm. " . " "		
4: 26	125		18 mm. " . " "		
4:27	110		nothing		
4: 28	125		20 mm. " . " "		
	0.05 gram of M.G.S. per Kilo. subcutaneously.				
4:29	125		20 mm. fall. (missed beat)		
4:30	110		5 mm. " .		
4:31	125		20 mm. " . " "		
4:32			4 -	15. Volts	
			2 -	12.	
			0	10.	
			3 -	12.	
			3 -	13.	
			2 -	12.	
			0	10.	
			slight	11.	
4:35	62		nothing		
	125		30 mm. fall. (missed beat)		
4:37	0.05 gram of M.G.S. subcutaneously.(per Kilo).				
4:38	110		8. mm. fall		
	125		27. mm. fall (M.B.)		
4:40			2 -	12. Volts	
			1 -	11.	
			0	10.	
			4 -	15.	
4:45	0.15 gram of M.G.S. per Kilo. intravenously.				
4:46	125		nothing		
4:48	225		19 mm. fall (M.B.)		
4:51	225		8.mm. " . 2 -	12.Volts	
			4 -	15.	
			1 -	11.	
			0	10.	
4:55	225		slow conduction After Affect. 18 mm. fall (M.B.)		
5:10	225		S.C. & L.A. 13 mm. fall (M.B.)	same as at 4:51.	

Animal Died of respiratory failure.

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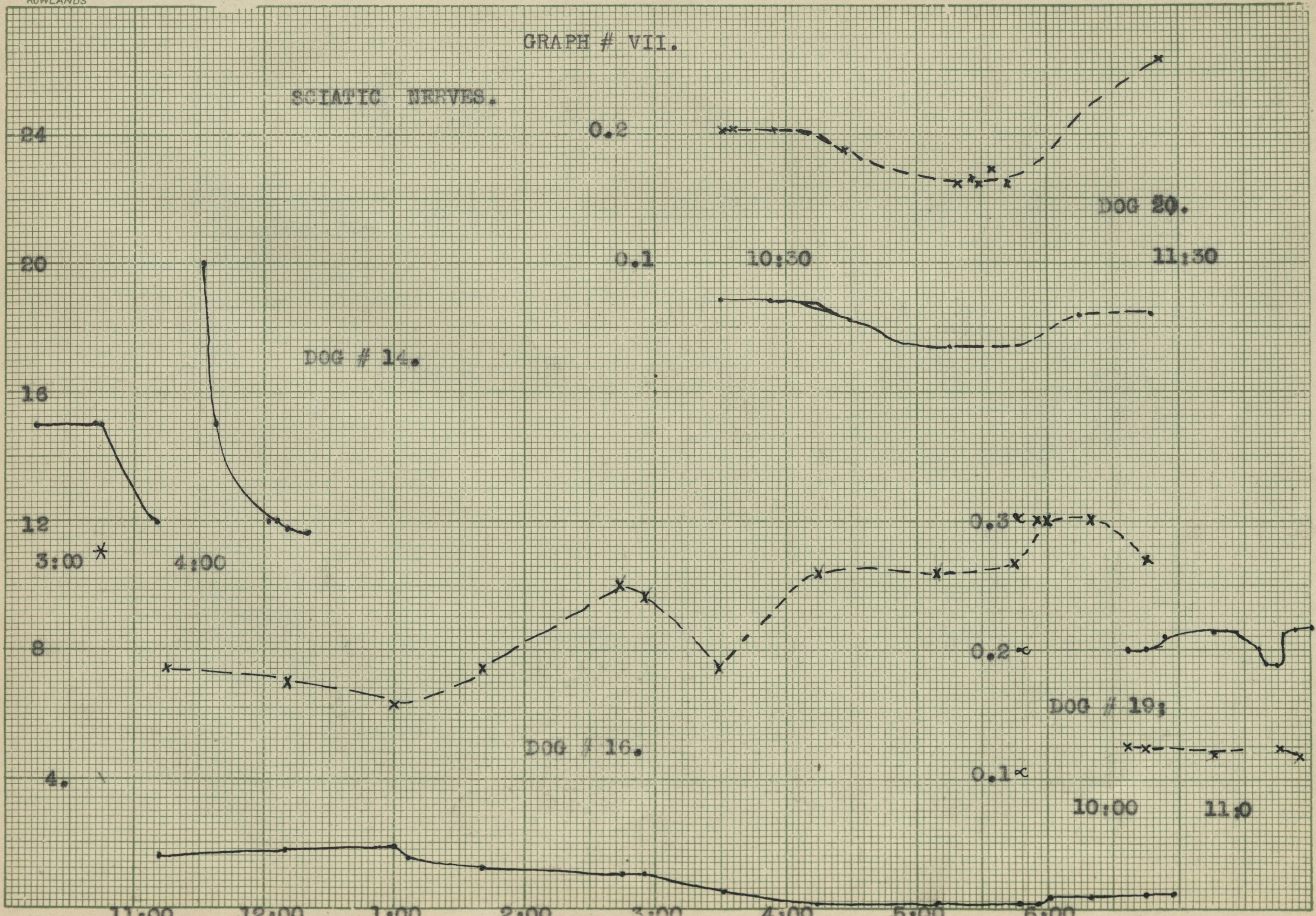

GRAPH # VII.
SCIATIC NERVES.
0.2
0.1
10:30
11:30
DOG 20.
24
20
16
12
8
4.
DOG # 14.
3:00
4:00
0.3
0.2
0.1
DOG # 19;
10:00
11:0
DOG # 16.
11:00
12:00
1:00
2:00
3:00
4:00
5:00
6:00

DOG # 16.

Weight - 13.4 Kilos.

Performed May 3 , 1928.

Ether started at 11:04 A.M.

	Sciatic Nerve.		Left Vagus Nerve.		
Time	Rheobase	Chronaxie	Rheobase	Sigma.	Response.
11:12	1.4 Volts.	.185			
12:10	1.82	.185 -			
12:20			92.		10. mm.
12:40			118.		10. ".
1:00	1.82	.148 —			
		.185 -			
1:10			118.	.185	10.mm.
1:30			118.	.185	4 mm.
2:05			130.	.185	4 mm.
2:20			130.	.185	6 mm.
			130.	.1156	5mm.
2:00	By feeling not seeing the contraction.				
	.1	.259	Possibly a different muscle.		
2:12	0.95	.185			
	Ulnar nerve - Toes movement.				
2:40	1.	.266			
3:00			100.	.185	5.mm.
3:40	Sciatic Nerve. (gastrocnemius)				
	0.5	.185			
4:00			67.	.185	2. mm.
4:15	Ulnar Nerve - toe Movement.				
	0.17	.259			
4:25			130	.185	M.B.
5:10	0.18	.259	55.	.185	4. mm.
5:30	0.15	.2664			
5:40	0.14	.3			
5:45	0.1 gm. M.G.S. per Kilo. intravenously.				
5:50	0.3	.3	130	.3	no response.
6:00	0.35	.3	150	.185	n0 response.

****

Dog # 19.

Female, Weight - 12 Kilos.

Performed April 3, 1928.

Ether started at 9:52 A.M.

	Sciatic (Ulnar)		Vagus Nerve(Left)		
Time	Rheobase	Chronaxie	Voltage	Sigma	Response.
10:06	8. Volts	0.123			
10:15	8.	0.123			
10:40			Rh. is 50. Ch. is 0.3 +		
10:43			55	0,185	4. mm.
			55	0.148	3. +
			90	0.07	3. +
10:45	8.5	0.1156			
		(15 Volts 0.3)			
10:56		0.025 grams of M.G.S. per Kilo. subcut.			
10:57			54	3.	slight.
10:58			64	"	4. mm/
10:58½		0.025 grams og M.G.S. per Kilo. subcut.			
10:59			64	3.	4.
11:00			64	"	5.
11:03	8.5				
11:04		0.1 gram subcut. of M.G.S. per Kilo.			
11:06	8.				
11:07			54	3.	2.5
			64	3.	5.
11:08	7.5				
11:09			54	"	7.
11:10			65	"	11.
			34	"	8.
			44	"	8.
11:12			Rh is 44. Ch. is 0.07-		
11:15	7.5	0.123-			
11:17		0.1 gram of M.G.S per Kilo. intravenously.			
11:18½	8.4	0.1156 -			
11:21			54	3.	2.
11:22			63	"	8.
11:23	8.6				
11:32	8.6				
11:35		Animal died of respiratory failure.			

DOG # 20.

Male ,Weight 11 Kilos. White Terrior.

Large M.G.S. intravenous injections for its effect upon the sciatic nerve in particular.

Time	Sciatis Nerve. Rheobase	Chronaxie.	Left Vagus Nerve. Rheobase	Chronaxie.
9:30	Ethere startdd.			
10:00			32. Volts.	.185
10:15			34	.185
10:20	2.8 several checks.	.203		
10:28			36.	.185
10:35	0.15 gm. M.G.S. per Kilo. intravenously.			
10:38			145.v.very slight.	
10:39	2.2	.185		
10:47	0.3 gm. M.G.S. per Kilo. intravenously.			
10:52	1.7	.148 to .185		
10:58	Animal in tetany.			
11:04	0.15 gm. M.G.S. per Kilo. intravenously.			
11:10	Animal in tetany.			
11:12			145. v.v. slight.	
11:15	2.2	.259		

****

Dog #1.

Female Weight 10 Kilos.

Performed December 19, 1927.

Vagus seemed to be very active shown when it was cut.

Time.	Vagus Rheobase	Vagus Chronaxie	Chordae Tympani Rheobase	Chordae Tympani Chronaxie
10:30		Ether started		
11:00			11. Volts	0.08-
11:10	30	0.07-		
11:15			7.	0.08-
11:30	40	0.07-	7.	0.08-
11:35	40	0.07		
11:38		o.025 grams of M.G.S. per Kilo. subcut.		
11:39	40	0.07		
11:41	42			
11:43			12.	0.07---
11:50	40	0.07		
11:55		0.05 gram of M.G.S. per Kilo intravenously.		
12:10	37	0.08-	50.	

Dog # 2.

Male Weight - 23 Kilos.

Performed December 20, 1927.

Time	Vagus Rheobase	Vagus Chronaxie	Chordae Tympani Rheobase	Chordae Tympani Chronaxie
10.30		Ether Started.		
10:55	260 Volts gave no response		9 .	0.07 --
11:05	260 " " " "		9.	0.07-
11:10		0.05 grams of M.G.S. per Kilo intravenously.		
11:12	260 - no response		9.	0.07
11:20	260 - no response		45.	0.07
11:22			50.	0.07
11:25	260 - no response.			

FROGS.

Frog # 16 (Nerve muscle preparation).

Rheobase = .06 Chronaxie .3 sigma sec.

0.1 gm. of M.G.S. in ringers dropped upon Nerve .

Rheobase = 2. Chronaxie - .185 -

****

Frog # 12 .

Rheobase - 0.46 volts Chronaxie 0.3 sigma sec.

M.G.S. into dorsal lymph ~~sack~~ region .

Rheobase and Chronaxie same after 10 seconds.

4 minutes Rheobase decreased and Chronaxie - .185

10 mintes Rheobase augmented.

****

Frog # 14 .

Rheobase 0.6 Chronaxie .3

M.G.S. into the heart caused slowing of heart .

Rheobase augmented .

****

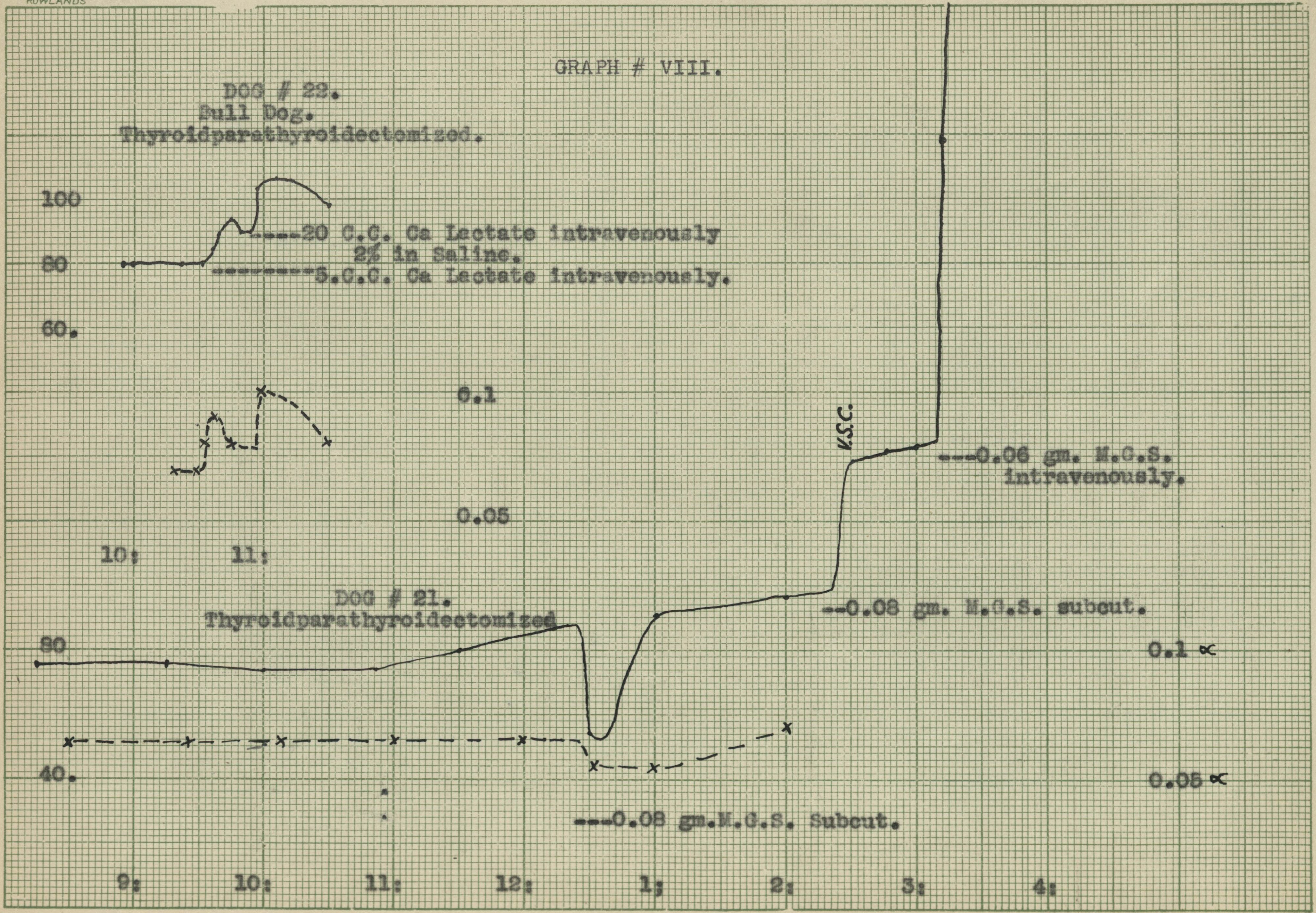
Frog # 21 .

Rheobase of muscle - .05 Chronaxie ~~xxx~~ .3
of nerve - .05 " .3

M.G.S. into blood in the heart .

Rheo of Muscle - Chronaxie of muscle
Rheo of Nerve .8 Chronaxie Nerve - .185

Probably here the nerve ending instead of the muscle was stimulated.


GRAPH # VIII.
DOG # 22.
Bull Dog.
Thyroidparathyroidectomized.
100
80
60.
---20 C.C. Ca Lactate intravenously
2% in Saline.
---------5.C.C. Ca Lactate intravenously.
0.1
0.05
10:
11:
DOG # 21.
Thyroidparathyroidectomized
80
40.
---0.06 gm. M.G.S.
intravenously.
--0.08 gm. M.G.S. subcut.
0.1 ∝
0.05 ∝
---0.08 gm.M.G.S. Subcut.
9:
10:
11:
12:
1:
2:
3:
4:

DOG # 22.

Bull Dog.

Date.	Wt.	Heart Rate.	Resp. Rate.	Operation.
4/4/1.	15.4	127.	Panting, a hot day.	
4/2		136	26.	
4/3	15.2	117		
4/4				L. Sciatic cut high.
4/6		156	L. inguinal gland swollem.	
4/11	15.	161	" " " " (lest).	
			27.	
4/12	15.			Thyroidparathyroidectomy.
4: P.M.				
4/13	4/15 P.M.	139.		
4/14	4: P.m.	88.		Muscle tremors slightly.
4/15	11: A.M.	110.		No Tremors.
4/17		87.		Tremors except cut Sciatic.
4/18		84.		" " " "
4/19		81.	Increased	" " " " "
4/21		78.	"	" " " " "
4/23	15.	73.	17.	Ditto.
4/24		56	15.	Ditto very marked.
4/26		56	15.	Ditto Ditto.

Animal etherized and irritability of the Vagus determined.

****

Time	Rheobase	Chronaxie	Response Rh.	Response Ch.	Intravenous Injection, gm. per kilo.
9:45			Vagus tied	- Active.	
9:55	80.	0.07	8. mm.	8. mm.	
10:00	85.	0.07	12.mm.	13. mm.	
10:20	85.	0.07	14.mm	14 mm.	
10:30	85	0.07	14 mm.	14 mm.	
10:33					0.007 Ca.Lactate
10:34	85.	0.07	6 mm.	2 mm.	
1o:38	90.	0.082	8 mm.	6 mm.	
10:45	95.	0.082	8.mm.	8 mm.	
		0.092		M.B.	
10:48	90	0.092	9.mm.	9 mm.	
10:53					0.028 Ca.Lactate.
10:54	104.	0.1004	8 mm.	9 mm.	
11:05	140.		8 mm.		
11:30	1o8.	0.08	14 mm.	15 mm.	
		0.092		Missed Beat.	

****

DOG # 21 .

Fox Terrior.

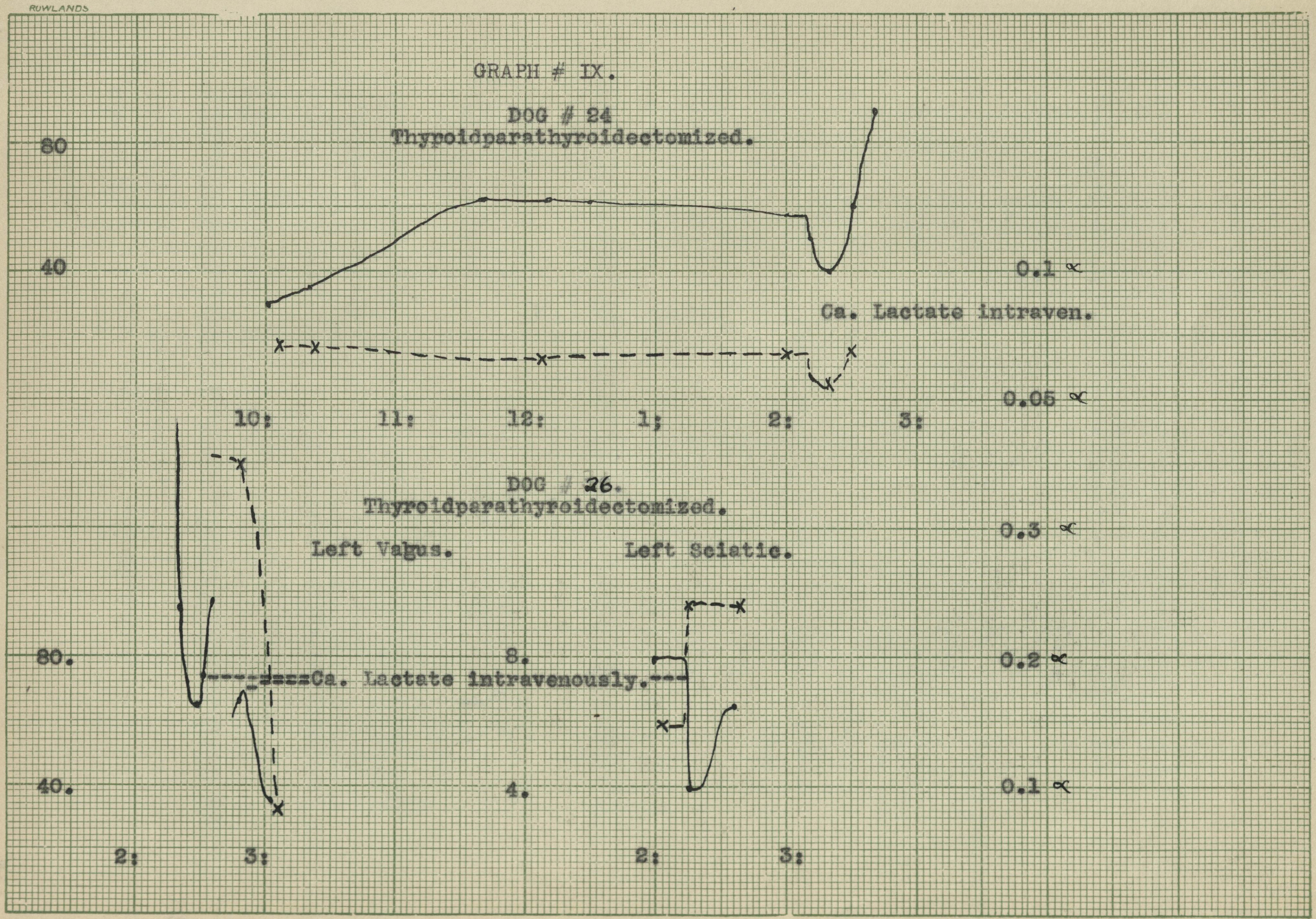
Date	Heart R.	Resp. R.	Wt.	Observations or Operations.*
4/1	84	19	9.5	
4/2	92	16	9.48	Tremors easily by fright.
4/3	79	17	9.5	
4/12	84	18	9.5	Thyroidparathyroidectomy 5;30 P.M.
4/13	87	19		**************************
10: A.M.				
5:p.m.				after walking him, tremors & inc. tone.
7;p.m.	176			fairly stiff, jerkings, tremors, increased salivation. NO TETANY.
7:30				Etherization started.
8:20	186			Mean blood pressure -- 154.
8:25				Vagus ligated. ---------- Active.
8:26				Mean blood pressure 180.
8:40				" " " 134. constant.

****

Time	Rheobase	Chronaxie	Responses RH.	Ch.	Maximal Stimulus.	gm.M.G.S. inj. per Kilo.
8:45	74.	N.	6 mm.			
9:15	74.	0.07 --	6.mm.	16.		
10:00	70.	0.07 --	5.mm.	10.	0.09	
10:30	70.	0.07	12.	34.		
11:30	80.	0.08----	10.	30.	0.09	
12:25						0.08 Subcut.
12:30	64.	0.07-----	8.	28.	0.09 - N.D	
1:00	90.	0.07 --	9.	20.		
2 :00	100.	0.07	20.	19.	Sluggish conduction.	
2:20						0.08 Subcut.
2:30	160		20.		Slow conduction & after affect.	
2:45	160		20.			
3:00	220		30.		0.08 -	
3 :10						0.06 intravenous.
3:11	220		2.		0.07 -	
3:15	220		2.			
3:30	220		2.		0.070 -	

Long Deep respiration inmediateky after the injection of the methyl guanidin sulphate , FIRST INJECTION.

****


ROWLANDS
GRAPH # IX.
DOG # 24
Thyroidparathyroidectomized.
80
40
0.1 α
Ca. Lactate intraven.
0.05 α
10:
11:
12:
1;
2:
3:
DOG # 26.
Thyroidparathyroidectomized.
Left Vagus.
Left Sciatic.
0.3 α
80.
8.
0.2 α
Ca. Lactate intravenously.
40.
4.
0.1 α
2:
3:
2:
3:

Dog # 23.

White Dog.

May 2nd. Thyroidparathyroidectomy.

May 4th. 3: p.m. Tremors, mild tetany.

5:30 p.m. Tetany Convulsions.

5:35 p.m. Ether was started.

5:42 p.m. Sciatic nerve (Ulnar Nerve).

toe Movements ; Rheobase = 0.1 Volt.

Chronaxie = 0.259 sigma.

5:50 p.m. L.Vagus nerve (12 mm. fall).

Rheobase = 43. Volts.

Chronaxie = .07 --- sigma.
(.061 sigma).

Max. Stim.= .1156 sigma.

Dog # 24.

Scotch Collie, Female.

Date	Time	Wt.	Heart R.	Resp. R.	Operation & Notations.
4/1		13.7	93	44	
4/2	11:A.M.		86	32	
4/3		15.6	80	36	
4/4					L. Sciatic cut HIGH.
4/11			86.		*********************
4/12	5:30 P.M.				THY.parathyroidectomy.
4/13	4;P.M.		126		Nose swollen some
4/14	4:p.m.		84		
4/15	11:a.m.		104		
4/16	11?a.m.		102		Slight tremors.

****

Time	Rheobase	Chronaxie	Response Rh.	Response Ch.	Maximal Stimulus	Gm.per Kilo. Ca.lactate intravenous.
10:00	30.		10 mm.			
10:05	30		10 mm.			
10:06		0.07 -		14mm.		
10:20	35	.07 -	10 mm.	14 mm.	.092 -	
10:40	60					
12:10	60	.07 --	7 mm.	12 mm.		
12:30	60		7 mm.			
2:00	50		7 mm.		.1156 --	
2:09½	50		7 mm.			
2:10						0.02
2:10½	50		10 mm.			
2 :20	40		12 mm.			
2:30	60	.07 *--	5mm .	16 mm.	.185	
2:40	90 *	.07-- *	14 mm.	18 mm.	.123 --	

****

* means Missed Beat.

Dog # 27 .

Rat Terrior.

May 12th. Wt.- 14. Kilos. Thyroidparathyroidectomy .

May 14th. Tremors first appeared.

May 17th. 8: a.m. Tetany.

10:30 a.m. Started to administer Ether.

The animal took a few breathms which removed the restraining action of the higher centers. This caused increased tetahy and respiratory stoppage. Artificial respiration was needed for one hour. Brain had become anemic.

* No further ether was given to this animal.

Left Vagus Nerve :

Time	Rheobase	Chronaxie	Response. RH.	Ch.	
11:00	35.	0.09	10 mm.	8. mm.	MISSED BEAT.
		o.1156		12 mm.	" " .
11:30	47.	0.148	22 mm.	20 mm.	" " .
11:35	48	0.148	22 mm..	21 mm.	" " .
11:45	Artificial respiration withdrawn. Animal breathimg				
12:10	35	0.148	20.mm.	20 mm.	MISSED BEAT.

SCIATIC NERVE (ULNAR) toes movement.

Rheobase = 1. Volt. Chronaxie = .135 sigma.

12:25	40.	0.148	20 mm.	19 mm.	MISSED BEAT.
12:30	47	0.148	20 mm.	20 mm.	Missed Beat.

****

Dog # 26 .

Terrior Pup.

May 12th. Wt.- 3.8 Kilos. Thyroidparathyroidectomy.

Heart Rate = 89 per minute.

May 14th. Tremors fairly strong.

May 16th. 3:30 Slight tetany.

7:30 Tetany Convulsions.

May 17th. 8:30 a.m. No tetany convulsions , Back arched, Dog groaning and in a depressed condition . Walked stiff legged and poor equilibrium .

1:38 P.m. Ether started.

Time	L. Vagus . Rheobase	Chronaxie	Response	L. Sciatic (Ulnar) Rheobase	Chronaxie .
			Rh. Ch.		
1:55	78.	.185	5 mm. 4 mm.		
		.259	4 mm.		
			L.A. & S.C.		
1:58	78.		2 mm.		
2:00				8.	.148
2:05	135.		v. very slight.		
2:18	0.18 gm. Ca. Lactate per Kilo. intravenously.				
2:15				4.	.240
2:17	135.		85 mm. M.B.		
2:20	95.	.3 ——	26 mm. M.B. 18 mm.		
2:25	75.		Slight.		
2:26	0.06 gm. Ca. Lactate per Kilo. intravenously.				
2:28	65.	.4 ——	28 mm. M.B. 21 mm.		
2:33	74		30 mm. M.B.		
2:36	97.		26 mm. M.B.	6.5	.240
	Electrodes put on Right Vagus.				
2:45	64.	.4625	10 mm. M.B. 10 mm.		
2:50	0.32 gm. Ca. Lactate per Kilo. intravenously.				
3:05	35.	.082	14 mm. M.B. 10 mm.		

****

One of the animals of group L.

Dog $ 11,

Black and White Dog. Wt. 5. Kilos.

Heart Rate - 100.

Experiment performed April 4th, 1928.

11:30 a.m.	Cut the Left Sciatic Nerve.
9: p.m.	Heart Rate = 103.
09:35 *	0.05 grams M.G.S. per Kilo. subcutaneous. L.side
9:45	Restless and whining, Increased tonus left side
9:50 *	0.03 gm. M.G.S. per Kilo subcutaneous right side.
9:55	Sneezing and rubbing nose.
9:58	Heart Rate = 62. per minute. more sneezing, and rubbing of the nose.
10:00	Restless, rubbing nose, whiming.
10:04	Both side balance each other , whining and rubbing of nose , Restless, Bladder relaxed while laying down.
10:05	Face swollem and the eyes swollen somewhat shut.
10:07	Abdominial muscles taunt , Ani sphincter and vagina sphincter contract and relax.
10:15	Muscle tonus increase except in the L. leg.
10:20	Slight tremors in legs particularly except in the Left leg.
10:24	Whining , cross , slight tremors , long difficult expiration and short inspirations.
10:25	Vomited , previously sounds from movement of the digestive tract heard.
10:27	All legs show much tonus increase except left leg . Eyes shut , nose swollen , rubbing it.

10:35 Same as 10:27 . Vomited again.

10:40 Vomited again.

10:50 L.leg seems colder than the others , Inc. tonus.

10:55 Animal is resting easier.

11:00 Tetany for 1½ minutes, Walking Mechanism involved.
No tremors in the left leg.

11:04 Pulse taken ,= 60 to 65 per minute.

11:07 Another spasm of tetany, same as 11;00.

11:10 Another spasm ot tetany, same as 11:00 .

11:12 Another spasm.

11:15 A Another spasm. probably one long spasm of tetany decreased at times due to decreased respiration during the hieghts of the tetany convulsions.

11:17 Heart Rate is 85 to 90 . soft weak pulse.

11:23 Another real spasm started by the animal starting to walk backward. Everywhere but in the L. leg. Similiar to the convulsions of 11:00 to 11:15 .

11:27 Animal died from a stoppage of respiration. the heart beat continuing for a few minute longer.

* Denotes an injection.

****

Dog # 12 .

Brown and white dog Male, Wt. 16 Kilos.

January 16 , 1928 Right Sciatic Nerve cut.

February 1st, 1928.

2:30 * 0.1 gm. of M.G.S. per Kilo. intravenously.
Immediate increase in respiration.

2:32 Walked restlessly, looking sickly .

2:33 Pupil dilated , increased tone , Laid on side with legs extended except right leg. Incresed salivation.

2:35 Sphincter ani relax , defecated , Walked restlessly and whined continually.

2:48 Acted as if he wanted to sleep, still much flow of saliva .

3:00 Started walking, restless, whining, tonus increased.

3:10 Laid down again .

3:20 Picked dog up from where he was lieing , very poor sense of equilibrium .

3:20½ Started to walk backward and then went into a spasm of tetany convulsions for 3 minutes.

3:24 Got up, walked, restless; Diarrhea intermittently but continuously for 5 minutes.

3:50 Tired and sleepy . Still increased tone except in the right leg . Salivation still marked . Nose swollen, rubbing it frequently .

4:20 Mucous congestion in the nose .

February 2 , 1928.

10:00 Mucous congestion in nose which was swollen. Resembling a bad cold . Diarrhea.

February 8th, 1928.

Animal condition simillar to that on the 2nd. yet not so severe. The animal was then killed.

****

Dog # 10 .

Brown and White. Male Wt. = 13.2 Kilos.

January 31st , 1928.

Right Sciatic Nerve cut high .

Feb. 3rd , 1928.

10:58 * 0.1 gm. M.G.S. per Kilo. Intravenously. Marked immediate respiratory increased.

11:00 Stood up , felt sick , balance poor. Saliva flow markedly increased, pupils were dialated, Tonus increased.

11:02 Tetany convulsions for 2 minutes involving the walking mechanism of the front legs . Jaws were continually contracting as if biting or chewing . No tonus increase in leg of cut sciatic.

11:10 In walking, his sense of equilibrium was not functioning properly .

11:12 Tetany and spasm for 1½ minutes , as at 11:02 .

11:14 Seemed tired . Defecated and urinated .

11:15 Very uncomfortable , restless , poor balance , over reaching , slow in action.

11:20 Started rubbing his nose which was larger than normal . An increase mucous secretion for some time. Eyes kept shut . Pupil dialated ?

11:30 Diarrhea .

February 10th, 1928.

Observation during this week showed the symptons continue of diarrhea and swollen nose .

February 21st, 1928.

The symptons still were present. The animal was killed .

****

Discussion of Results .

The animals of group VIII show that following the ligature of the vagus , there was a gradual rise of its rheobase without any change in its chronaxie. This shows that the vagus resembles the somatic nerves in this characteristic , which Lapicque showed the sciatic nerve possesed this same property . That is the separating of a nerve from the central nervous system causes its rheobase to increase with no change in the chronaxie .

In the decerebrated animal , # 25 , the rheobase was 100 volts immediately after tying the vagus . Three hours later the intensity necessary to stimulat was 220 volts. See results Graph I , page 14 . On the same graph are recorded the results of Dog # 13. Here the original rheobase was 43 volts and this increase to 86 volts in 1½ hours , the chronaxie remaining between 0.07 and 0.082 sigma seconds .

Noting Dog # 28 , page 21 , the rheobase ten minutes after ligating the vagus was 65 , then occurs a gradual rise until after an interval of 1¾ hours the irritability has decreased ~~xxxxx~~ so that 100. volts are necessary to bring about a response. In this time interval the chronxie remains at 0.148 sigma seconds .

The results of Dogs # 21 , and 24 both thy-para-ect. dogs page 32 , show similiar increases ; the former changing from 74 to 85 and the latter rising from 30 to 60 volts .

A check upon this observation are the results of Dogs # 24 and 29 . Here determinations were made upon both vagi , one of them being ligated some time before the other one in the same animal . Forty five minutes preceding the tying of the right vagus, the left vagus was tied ; determinations were made upon both nerves within a five minute interval including shocks . It was found the rheobases were Right = 35., Left = 50. volts . In animal # 26 the difference in tying time was 1 hour , the rheobase difference was approximately 30 % .

The chronaxies of all the above animals did not show a variance to any extent at different time intervals.

As stated previously , it has been demonstrated that ether has an augmenting effect upon the rheobase and a diminishing effect upon the chronaxies of nerves . Quoting Buchanan and Garven (15) they find ether to augment both the rheobase and the chronaxie of nerves . These two findings do not agree in their affect of ether upon the chronaxie of nerves. These workers find the effect of the ether begins to appear in 20 to 30 minutes and last three to six hours following the administration. They state the effect completely disappears within 9 to 12 hours after the withdrawal of the ether .

Taking these observations, controls have been used to show that the method used in these experiments has removed by far the largest amount of the error induced with the use of ether .

Dog # 25 was decerebrated while under the influence of ether, the anesthetic was stopped at 11:40 a.m. Eleven and one half hours later the sciatic rheobase was 1.5 volts, and the chronaxie .2407 to .2601 sigma seconds . These determinations were made upon the vagus ten hours following the operation:- (1) to cause a slight fall in the blood pressure , Rheobase = 110. volts , chronaxie = .07 sigma ; (2) to cause a sudden drop of blood pressure due to a temporary missing of the heart (called missed beat) the requirements were R = 130 , C = .259 sigma seconds .

An experiment was performed where the E.E. was measured immediately following the administering of the ether . The anesthesia was started in dog # 29 at 10:40 . To cause a slight fall in the blood pressure, the rheobase was 81 at 10:50 , the chronaxie equaled .3 sigmas at 10:52 , and the rheobase was checked at 81 one half of a minute later.

The chronaxies of dog # 13 , 17 , 20 , 28 were constant for a time interval of 60 to 90 minutes, at which time they were used for experiments . The rheobases were gradually augmented in these animals due to its separation from the central nervous system. These results are evidence that the method use elimiates the administering of ether during the experiments does not influence the measurements of the irritability of the vagus nerve .

Additional proof is presented by animal # 27 , a thy-para-ect. dog , where no ether was given during the experiment . Upon the development of active tetany , the anesthesis was started upon this animal. A few breaths, which removed the normal restraining action of the central nervous system caused such an increase in the tonus and the tetany that respiration or even artificial respiration was impossible . By the time the abdominal muscles had relaxed so artificial respiration could be given , the nerve cells in the brain had been anemic long enought to interfere with their further activity . Consequently no more ether was given . It was necessary to carry on artificial respiration for nearly an hour, which was done by machine . After this time interval the respiratory centers of the dog again started to function. During this time the E.E. of the vagus and the sciatic nerves were measured. Then ether was given to the animal and the rheobase and chronaxies again were measured. No change occurred in the chronaxies of either nerve ; a slight rise was found in the Vagus nerve rheobase, which was ~~xxxxx bx~~ probably due to its ligature ; the rheobase of the sciatic nerve increased over three fold .

These animals , # 25 , 20 , 16 , & 19 , used to compare for the effect of the anesthesiax upon the E.E. of the sciatic show that the ether influence upon the rheobase was not completely overcome in these determination . Yet this influenced the determinations by making the rheobases higher than correct and did not influence the chronaxie to any amount that is of any inportance . To overcome any varying amount of this influence , an etherizing apparatus was used wherby the degree of anesthesia could be regulated accurately and easily . In this manner this variation was constant . The vagus was free from any influence of the ether probably because, this nerve was kept exposed to a better degree than was possible with the sciatic .

The method used was to expose the nerve immediately and maintain its exposure thru out the experiment ; yet protecting it from air currents and drying by covering it with cotton damp, but not wet with isotonic saline solution . The saline was not allowed to be in contact with the nerve due that it would then bring into the observations the salt content, which would influence the determinations .

In the rheobase estimations upon animals to which M.G.S. had been administered or following thy - para-ect., that is upon hyperirritable vagi , it was noticed that it was unnecessary to use a time interval of long duration . The time interval necessary was .09 to .3 sigma seconds; the more excitable the shorter time interval to give a maximal response for that voltage , the smaller the response the smaller the time interval necessary .

Attempting to measure this upon normal animal it was found to be very much higher and also varying for the different standard of amount of activity . This with observations of higher chronaxies in the same nerve of the same animal when a larger response is taken as the standard for the determination of the rheobase , leads to the conclusion that each nerve is made of neurones of various rheobases and chronaxies , those less irritable to intensity also need a stimulus of longer duration . The observations found upon animals # 25 and 30 imply that the above is the case ; in the former to cause a M.B. taken as a standard 150 volts and .259 sigma were the measurements , to cause a slight ~~fall~~ fall these were 110 and .07 sigma ; in the latter these were 140. - .240 sigma and 83. - .148 and a third standard of 10 mm. fell gave the measurements of 92. - .185- .

The administration of guanidin was subcutaneously or intravenously . At a scanning glance the effect of these two ways of injection seem to have just an opposite action upon the vagus . A closer interpretation shows the action is mainly one of degree rather than a difference .

In the thy-para-ect. animals the E.E. of the vagus was found to vary in the same manner as to the severity of the symptoms . This has been also demonstrated to not a difference of action , but one of degree .

The irritability of the vagus was determined upon eight dogs before and following subcutaneous injections of methyl guanidin sulphate . As shown in the composite table page 16 and in dog # 17 , a mark fall of the rheobase and the chronaxie occurs in all the animals . This is the action of small doses of guanidin as the absorption here is slow .

The vagus upon stimulation seems much more powerful and is very irritable. The difference between the measurements of the E.E. between a small response and a large response is very markedly decreased . This would inply guanidin action is more pronounced upon the neurones of high rheobases and chronaxies within the nerve . This would tend to bring all the neurones nearer together as to their irritability threshold .

Upon further subcutaneous injections , the fall of the rheobase and the chronaxie seems to occur much slower finally remaining constant for a short time ; and then the rheobase rises fairly quick,the chronaxie remaining about the same usually showing a small increase . This action is shown very clearly in dog # 17 , page 17 . This sudden decrease of irritability (rise of rheobase)following the initial hyperirritablity is in all probability a blocking as explained by Lapicque theory of iso-chronism,for here the chronaxie has been diminished to such an amount that blocking occurs. All of the neurones are blocked at about the same time which accounts for the sudden rise of the rheobase .

The point at which this blocking occurs seems to be when the chronaxie reaches 0.061 sigma seconds. This seems to be practically constant for all neurones in the vagus and for all vagi in animals studied .

Lapicque theory states that blocking occurs when the chronaxie decrease 50 % or to ½., here in the vagus it is noticed the decresed is to 1/5 to less . This inplies that two set of synapse or end plates are in the block. Further work will be towards locating its action on pre or postganglionic fibers or on both .

In intravenous injection the effect is inmediate due that all the guanidin is given at once . Consequently due to the rapid fall in the chronaxie , a block occurs before the period of increase excitability s can be demonstrated . In all animal where the administration is intravenously a marked decrease of irritability occurs . these animals include # 1 , 2 , 3 , 4 , 5 , 6 , 7 , 12 , 13 , 14 , and 20 .

In most of these animals the rise of rheobase was too large to measure the chronaxie. In animals # 3 , 7 , and 12 the chronaxies were found to be respt. as follows ; .068 , .06 -, and (estimated .059) sigma) .

The blocking was produced in 2 animals ,13 and 17 by subcutaneous injections , occurring when the chronaxies had been lowered to .061 and .068 repectively .

Results upon frogs showed a decrease in the chronaxie followed by a partial block of the sciatic in larger doses .

Relative to the effect of guanidin upon the sciatic nerve when injected subcutaneously , there occurs a lowering of the rheobase and the chronaxie yet it developes much slower and very much less then what occurred in the Vagus . Dog # 14 shows a 3 + response occurring at a voltage where it had been 2 + before the administration of guanidin . Upon continued subcutaneous injections (after the vagi becomes blocked) the rheobase was lowered to 11 volts . A similiar fall of the rheobase with no change in the chronaxie occurs in Dog # 19.. These results show the effect upon sciatic nerve is very small .

Using intravenous doses it was possible to show a typical action of the guanidin upon the sciatic as had been found with the Vagus with subcutaneous administration . The rheobase fell from 2.6 to 2.2 volts and the chronaxie decreased from .203 to .185 in dog # 20 following intravenous inj. of .15 gm. per Kilo (occurred in less than 4 minutes) . A second similiar inj. of .5 gm. caused the measurements to be 1.7 and .148 - . A third administration caused a increase of the measurements . In this animal the vagus gave its characteristic block caused by intravenous injection immediately following the first dose givemn .

Several dogs were used to find how the symptons of varying doses of M.G.S. correspond to those occurring min the different stages after the removal of the parathyroids .

The heart rate was decreased from 103 to 82 per minutes in dog # 11 after administering .05 grams per Kilos subcutaneously , this slowening occurring in 25 minutes . Another observation which is typical of increased vagus activity was that noticed in 29 minutes where the animal showed long difficult expiration probably due to the constriction of the bronchioles . Similier breathing was noticed in dog # 12 , but no particular observation was made upon the breathing of dog 10 . The remaining symptoms are very closely similiar to those recorded previously by other workers .

The parthyroids were removed from six dogs . Two of these were used previous to active tetany , yet while tremors of the muscles were occurring; one during slight tetany ; two during tetany ; and one in the partial depressed condition immediately following active tetany ; on all the E.E. of the vagus and on some of the sciatic were measured.

Dog # 22 showed a typical slowening of the heart from an average of 133 begore the operation to 88 on the second day , 110 on the third , and 56 on the ninth day following the operation . Measuring the E.E. of the vagus at this time the rheobase = 30 and the chronaxie = .07 . Literature states the symptoms develope slowly in Bull Dogs . The above determination shows the vagus to be hyperirritable .

A second dog , # 21 , upon shich the E.E. was measured just before active tetany developed showed upon ligating the vagus a very marked tonic action had been occuring (26 mm. rise) . Fifteen minutes later the rheobase was found to be 74 volts and the chronaxie less than .07 sigma seconds probably .066 . With the administration of guanidin subcutaneously the irritability increased in five minutes, the rheobase and the chronaxie both falling . By 35 minutes the nerve was near the blocking point as its action became sluggish and delayed , outlasting the duration of the stimulation . The rheobase increased while the chronaxie remained below .07 probably .064 . A second injection resulted in a strong block , occurring much quicker than in a normal dog as # 17 .

The third dog ,# 24 , measured while in light tetany showed a slight more active vagus than the preceeding animal, the the observations being 30 volts, and less than .07 probably .061 sigmas .

Animal # 23 and 27 vagi irritabilities were ascertained while the animals were in typical tetany convulsions . The former excitability was 43 volts and .061 sigmas second ; the latter measured, without the use of any anesthetic as described in page 45 , as 35 and.1004 to cause a M.B. with a fall of 10 mm. in the blood pressure - and 47 and .148 to cause a M.B. with a fall of pressure of 22 mm .

The measurements of the excitability of the vagus of an animal allowed to go into slight depression which occurs following the stage of active tetany, were 78 volts and .148 sigma second eight minutes after ligating the nerve, the same as it was three minutes after the tying. In twelve minutes the vagus showed a block, 135 volts causing only a slight fall.

Upon some of the thy-para-ect. dogs, the irritability of the sciatic nerve was taken. As Previously stateddog # 25, decerebrated, the irritability of the sciatic nerve measured 1.5 volts, .2407 to .2601 sigma sec. A dog in active tetany, # 23, also using no ether measured 1. volt, .128 — sigma second.

The irritability of the sciatic of dog # 23 taken during active tetany under anesthesia is much different, namely 8. volts, .289 sigma second. With the administration of Ca lactate this changed to 4 volts, .148 sigma second.

Summary of Comparisons.

The symptoms of subcutaneous injectionsof methyl guanidin and the early stages after thy-para-ect. resemble each other very closely if not identical in the modified condition of the vagus nerve. In both cases, it becomes hyperirritable, the rheobase, chronaxie, and maximal stimulus,all decreasing. Calcium Lactate overcomes this condition by decreasing the irritability, increasing the rheobase and chronaxie.

Large subcutaneous doses or small intravenous doxses of guanidin produce a condition resembling that of the vagus during active tetany following the removal of the parathyroids . Here , the chronaxie has been lowered to a point at which blocking has or is about to occur . With the establishing of the block the rheobase increase markedly and very rapidly . Small intravenous injections of Ca lactate will overcome this block by calcium lactate action of augmenting this lowered chronaxie .

Average intravenous injections of M.G.S. produce a block of the vagus due to the diminished chronaxie . The same block is found in the later part of active tetany and in the depressed stage following after thy-para-ect .

The irritability of the sciatic nerve is effected in a similiar manner , but very much less the blocking tendency not noticed until the depressed stage is reached .

The conclusions drawn by Buchanan and Garven (15) do not agree with results found herein upon the vagus or the sciatic nerves . This group of experiments was started aiming to the comparison of the irritability of of the vagus of animals in these two conditions . Due to the finding of what seemed to be contrary results to those of Buchanan and Garven, similiar observations were made upon the sciatic nerve .

In their comparison of guanidin animal to thy-para-ect. ones , it may be the symptoms of the two groups of animals are in the different degrees of severity .

A closer interpretation of their work with additional evidence obtained in these experiments inplies the error in their conclusion, if onee exists, is due to using too small of a dose of guanidin which does not effect the sciatic very marked , consequently they find no effect of guanidin upon the sciatic . Their results upon thy-para-ect. animals are not confirmed by the observations upon these dogs . The cause of the skeletal symptoms inthese conditions is probably a lowering of the chronaxies of nerves, the decrease being the more in the neurones in the central nervous system than that in the neurones in the peripheral nerves .

Conclusions .

1. The separation of the vagus nerve from the Central Nervous System causes its rheobase to increase 100 % in approximately an hour and a half , where it remains fairly constant . The chronaxie thru out this time does not vary to any extent .

2. A nerve is composed of neurones of various rheobases and chronaxies, the neurones with the higher rheobases also have the higher chronaxies .

3. Guanidin administered slowly as in subcut-aneous injections causes a progressive decrease in the irritability of the nerve as measured in rheobase and chronaxie , the effect being the more pronounced upon neurones of less irritability within the nerve.

4. This diminishing of the chronaxie if carried beyond a certain ,probably definite , point causes a blocking of the nerve thereby raising the rheobase . This point for the vagus lies between .061 and .o68 sigma seconds probably nearer the former .

5. Intravenous doses cause a block by the action of lowering the chronaxie .

6. The effect is much more pronounced upon the vagus than upon the ulnar nerve , usually not being observable , at least measurable until small intravenous injections are made . (in the ulnar nerve)

7. The irritability of these nerves are effected in the same manner following thy-para-ect .

8. Subcutaneous administration of .05 gm. of methyl guanidin sulphate per Kilo. cause symptoms which corresponds to those of stage of nervous twitches in parathyroidectomized animals .

9. Injection of .15 gm.per Kilo. subcutaneously or .05 gm. intravenously cause symptoms which correspond to the stage of advanced active tetany in a dog that has had the parathyroids removed .

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